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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,193	12/02/1999	SHIGENORI OHKAWA	2470US0P	9630

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TAKEDA PHARMACEUTICALS NORTH AMERICA, INC
INTELLECTUAL PROPERTY DEPARTMENT
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EXAMINER

ROBINSON, BINTA M

ART UNIT	PAPER NUMBER
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1625

DATE MAILED: 12/18/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/445,193

Applicant(s)

OHKAWA ET AL.

Examiner

Binta M. Robinson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5,8-15,22,24-26 and 28 is/are pending in the application.

4a) Of the above claim(s) ____ is/are withdrawn from consideration:

- 5) ☒ Claim(s) 24 is/are allowed.
- 6) ☒ Claim(s) 1-3,5,8-15, 22,24, 25,26 and 28 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other:

Detailed Action

(Revised rejection)

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

¹¹⁻¹⁵
Claims ~~4-3, 5, 8-15~~, and 22 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record at paper no. 13, because the specification, does not reasonably provide enablement for R4 being other than the moieties claimed on pages 103-105, and ~~R3 being other than phenyl substituted with the groups delineated in the 103-105.~~ The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement for reasons of record at paper no. 15. The applicant does not enabled R3 equal to phenyl substituted with 2 or more electron withdrawing groups in the ortho position or R4 equal to C1-4 alkyl groups substituted with phenyl or pyridyl which is optionally substituted 2 or more electron withdrawing groups in the ortho position.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the

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invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art 6) the amount of direction provided by the inventor 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In *re Wands*, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In terms of the first Wands factor of breadth, R4 can be an aliphatic hydrocarbon group substituted with aromatic groups other than those depicted on pages 103-105, and R3 can aromatic groups other than the substituted phenyl rings depicted on pages 103-105; in terms of breadth an array of unrelated diseases ranging from Alzheimer's disease to Huntington's chorea are claimed. In terms of the nature of the invention, which is the second Wands factor, these compounds are used as agents for suppressing neurodegeneration. In terms of the fifth Wands factor, Cell-protecting activity ranges from 30.7 % to 47 %. There are significant differences in cell protecting activity for small changes in structure. For example, compounds 1 and 25 on pages 103 and 104, differ at the e moiety. For compound 1, e is benzyloxy; for compound 25, the e moiety is benzylmethoxy. However, the cell protecting activity for compound 1 is 30.7 % and for compound 25 is 47%. The level of predictability regarding cell protecting activity is low. In terms of the sixth Wands factor, the amount of direction provided by the inventor is poor, because the applicant only tests 7 compounds with very limited markush groupings, whereas Y, R4, and R3 encompass broader Markush groupings. The applicant has only tested Y equal to oxygen, R3 equal to substituted phenyl, and R4 equal to the groups depicted on pages 103-105. These

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working examples do not encompass the entire scope of Y, R3, and R4.

Additionally, these various compounds have not been tested

Alzheimer's
for their affects on the ~~various diseases~~ claimed in claim 28. In terms of the 8th

Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of predictability in the art of the invention, and the poor amount of direction provided by the inventor. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for R4a being other than the moieties claimed on pages 103-105, and R3a being other than phenyl substituted with the groups delineated in the specification ~~and for the method of treating all of the various diseases, many of which are unrelated for reasons of record at paper no. 13. Alzheimer's Disease, which is mediated by serotonin, dopamine, and choline is unrelated to Parkinson's disease, which is a disease where the tremorine compound is diminished. There is currently no known treatment for amyotrophic lateral sclerosis. If Huntington's chorea is not detected in the fetal stage, it can't be treated. There is~~

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insufficient data in the specification showing how Huntington's chorea can be treated when this disease is often undetectable until the mid-30s, if not caught in the fetal stages. It is known that blood flow to tissues in diabetic neuropathy is impeded. The specification does not address how pharmaceutical treatments of diabetic neuropathy can be effective in light of the fact that blood flow to tissues is impeded. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art 6) the amount of direction provided by the inventor 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In *re Wands*, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In terms of the first *Wands* factor of breadth, Y can be S as well as O, R4 can be an aliphatic hydrocarbon group substituted with aromatic groups other than those claimed on pages 103-105, and R3 can aromatic groups claimed other than the substituted phenyl rings depicted on pages 1-3-105; in terms of breadth an array of unrelated diseases ranging from Alzheimer's disease to Huntington's chorea are claimed. In terms

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of the nature of the invention, which is the second Wands factor, these compounds are used as agents for suppressing neurodegeneration. In terms of the fifth Wands factor, cell protecting activity ranges from 30.7 % to 47 %. There are significant differences in cell protecting activity for small changes in structure. For example, compounds 1 and 25 on pages 103 and 104, differ at the e moiety. For compound 1, e is benzyloxy; for compound 25, the e moiety is benzylmethoxy. However, the cell protecting activity for compound 1 is 30.7 % and for compound 25 is 47%. The level of predictability regarding cell protecting activity is low. In terms of the sixth Wands factor, the amount of direction provided by the inventor is poor, because the applicant only tests 7 compounds with very limited markush groupings, whereas Y, R4, and R3 encompass broader Markush groupings. The applicant has only tested Y equal to oxygen, R3 equal to substituted phenyl, and R4 equal to the groups depicted on pages 103-105. These working examples do not encompass the entire scope of Y, R3, and R4.

Additionally, these various compounds have not been tested for their affects on the various diseases claimed in claim 28. Additionally, the applicant does not test the effect of these compounds on the specific diseases claimed. In terms of the 8th Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of predictability in the art of the invention, and the poor amount of direction provided by the inventor. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

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(oldrejection)

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

✓ Claim 25 is rejected under 35 U.S.C. 112, first paragraph, because the specification, does not provide enablement for R1 and R2 of the compound of formula I coming together to form all heterocyclic unsubstituted or substituted rings. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement. The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. The applicant is referred to *In re Wands*, 858 f.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) which includes the incorporation of the 8 factors recited in Ex parte Foreman 230 USPQ 546 (Bd. Of App. And Inter 1986).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the

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level of predictability in the art 6) the amount of direction provided by the inventor 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In *re Wands*, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In terms of the first Wands factor of breadth, R1 and R2 come together to form a whole Markush grouping of heterocyclics other than the piperidines depicted in the specification. In terms of the nature of the invention, which is the second Wands factor, these compounds are used as agents for suppressing neurodegeneration. In terms of the fifth Wands factor, cell protecting activity ranges from 30.7 % to 47 %. There are significant differences in cell protecting activity for small changes in structure. For example, compounds 1 and 25 on pages 103 and 104, differ at the e moiety. For compound 1, e is benzyloxy; for compound 25, the e moiety is benzylmethoxy. However, the cell protecting activity for compound 1 is 30.7 % and for compound 25 is 47%. The level of predictability regarding cell protecting activity is low. In terms of the sixth Wands factor, the amount of direction provided by the inventor is poor, because the applicant only tests 7 compounds with very limited markush groupings, whereas Y, R4, and R3 encompass broader Markush groupings. The applicant has only tested Y equal to oxygen, R3 equal to substituted phenyl, and R4 equal to the groups depicted on pages 103-105. These working examples do not encompass the entire scope of Y, R3, and R4.

In terms of the 8th Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the

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breadth of the claims, the level of predictability in the art of the invention, and the poor amount of direction provided by the inventor. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

Claim 24 is allowable.

The references that have been lined through in the IDS dated 12/2/99, still have not been considered because they have not been provided to the examiner.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (703) 306-5437. The examiner can normally be reached on M-F (9:30-6:00).


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on (703)308-4698. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-7922 for regular communications and (703)308-7922 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0193.

Binta Robinson



December 13, 2002


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